REMARKS/ARGUMENTS

As an initial matter, Applicants wish to thank the Examiner for reconsidering the restriction requirement and indicating that SEQ ID NOS: 8, 19, 20, 17, and 21 would be examined in the present application.

In the present response, Applicants have canceled claims 1-22 and added claims 38-52. Claims 38-52 add no new matter. Support for claims 38-51 can be found, for example, in the claims as originally filed. Support for claim 52 can be found, for example, in the specification on page 27, line 20 to page 30, line 20. Applicants reserve the right to pursue the subject matter of canceled claims 1-22 in one or more continuing or divisional application. After entry of the present amendments, claims 38-52 will be pending and under examination.

Trademark Objections

The use of the trademarks in the application is objected to for not including published product information sufficient to show that the generic terminology or the generic description is inherent in the article referred by the trademarks. Applicants respectfully traverse this objection.

According to MPEP 608.01(v), trademarks are permissible in patent applications, if one of the following two conditions are met:

(1) Their meanings are established by an accompanying definition which is sufficiently precise and definite to be made part of the claim, ***or***

(2) In this country, their meanings are well-known and satisfactorily defined in the literature.

Applicants submit that the drugs EPREX®, ERYPRO®, PROCRIT®, and NEORECORMON® are well known in the United States and are satisfactorily defined in the literature. Applicants therefore respectfully request that the objection be withdrawn.

Rejection under 35 U.S.C. § 112

Claims 1-22 are rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. To the extent the rejection applies to the claims as amended, Applicants respectfully request reconsideration of the present rejection because there is no evidence of record suggesting that a skilled practitioner would be unable to perform the claimed methods and achieve some measurable effect.

The initial burden to support an enablement rejection rests on the Examiner. In this regard, § 2164.04 of the MPEP states: "the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)(examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure)." MPEP § 2164.04 further states that a specification **must** be taken as being in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971)." The MPEP quotes *Marzocchi* as follows: "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure. 439 F.2d at 224, 169 USPQ at 370."

The present rejection does not satisfy the *Marzocchi* standard, as articulated in the MPEP. Rather, the Action sets forth only a general assertion that Applicants have not demonstrated that the claimed invention has a therapeutic level of efficacy and cites several articles discussing the difficulties inherent in treating neurological disease. In that manner, the Action identifies certain problems that allegedly would be encountered in practicing the claimed methods. There is no requirement in the patent laws, however, that patentable inventions be problem-free, or that a patent specification address all potential problems that might be encountered in practicing an invention. Notably, the claims at issue are not directed to curing or eradicating a disease state. The claims at issue are directed to methods for

treating a patient having a condition mediated by neurotoxicity, neurodegeneration, or neurological damage. The term treating can refer to *any indicia* of success in the treatment or amelioration of a condition.

The methods of the present invention use peptides that have been demonstrated by the present inventors to be EPO mimetics, *e.g.,* agonist peptides, capable of promoting neurite outgrowth in cells. The Action provides no evidence that a skilled practitioner, after reading the present specification, would be unable to administer a peptide within the scope of the claims, *i.e., a peptide capable of promoting neurite outgrowth*, to a patient and obtain a measurable effect, *i.e.,* neurite outgrowth in at least some nerve cells of the patient. To the contrary, the Bernaudin reference cited against the application (*Journal of Cerebral Blood Flow and Metabolism,* 1999, 19:643-651) demonstrates that the skilled practitioner is capable of using EPO to protect the brain from neurodegeneration. The Action provides no evidence that a skilled practitioner, after reading the present specification, would be unable to use EPO mimetics to promote neurite outgrowth in cells and thereby treat conditions mediated by neurotoxicity, neurodegeneration or neurological damage. The Action mistakenly asserts that the patent laws require that Applicant demonstrates the effectiveness of the claimed compositions in modifying the course of an illness. Enablement requires only that the application teach how to make and use the invention without undue experimentation. *See In re Sichert,* 566 F.2d 1154 (C.C.P.A. 1977). There is no reason to believe that one skilled in the art would be required to perform any amount of undue experimentation to administer the claimed compounds to a subject and achieve some measurable effect. Absent such evidence, the rejection for alleged lack of enablement is improper and should be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claims 1-22 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly unpatentable over Johnson *et al., Biochemistry,* 1998, 37:3699-3710, Bernaudin *et al., Journal of Cerebral Blood Flow and Metabolism,* 1999, 19:643-651; and Campana *et al., International Journal of Molecular Medicine*, 1998, 1:235-241.

As explained in the MPEP, to establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the

references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine their respective teachings. Second, there must be a reasonable expectation of success. Finally, the prior art references must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, not in Applicants' disclosure. *In re Vaeck,* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

The Office Action, however, fails to identify any motivation or suggestion in the cited references to use the peptides represented by SEQ ID NOS: 8, 19, 20, 17, and 21, and particularly SEQ ID NOS: 19, 20, 17, and 21, in the methods of the present invention. In fact, the Johnson reference, cited by the Action as teaching the peptides used in the present method actually ***teaches away*** from the present invention. As explained by the Action, the Johnson reference is directed generally to obtaining information about the functional importance of amino acids required for effective EPO mimetic action by identifying a minimal mimetic peptide sequence and by generating a series of truncation peptides. The authors of the Johnson reference using SEQ ID NO:8 as their reference sequence created more than 25 derivatives of SEQ ID NO:8 and evaluated them to determine whether they could act as EPO mimetics and activate the EPO receptor. Significantly, the authors found that several positions within the 20 amino acid sequence of SEQ ID NO:8 are integral for EPO receptor binding and mimetic activity. These positions are Tyr^4, Gly^9, Thr^{12}, and Trp^{13}. Notably, SEQ ID NOS:19, 9, 27, and 23 all have alanine substitutions at Tyr^4, Gly^9, or Thr^{12}. The authors found that alanine substitution of Tyr^4, Gly^9, or Thr^{12} in the derivatives each resulted in relative binding losses of manifold and a concomitant *loss of mimetic action* (page 3703, column 2). The authors also found that the two aromatic functionalities at positions 4 and 13 play especially important roles in receptor binding ability and EPO-mimetic properties (page 3703, column 2 to page 3704 column 1). Notably, SEQ ID NO: 19 is missing an aromatic functionality at position 4 and SEQ ID NO:17 and 21 are missing aromatic functionalities at positions 13. The authors also found that Tyr^4 must be retained in any truncated EMP1 derivative in order to function as an EPO mimetic. Notably SEQ ID NO:21 is a truncated EMP1 derivative without tyrosine at position 4. Accordingly, the Johnson reference teaches that SEQ ID NOS: 19, 9, 27, and 23 are all lacking amino acid residues essential for EPO mimetic activity. Although SEQ ID NO:8 is indicated as comprising all the

amino acid residues essential for EPO mimetic activity, there is no indication that the peptide can be used to treat a condition mediated by neurotoxicity, neurodegeneration or neurological damage. The Bernaudin and Campana references are cited for the proposition that EPO has neurotrophic activity. It is unclear however how a person of ordinary skill who did not have benefit of the hindsight provided by Applicants' disclosure would have attempted to combine the teachings of the Johnson reference with the Bernaudin and Campana reference. The Johnson reference teaches that SEQ ID NOS: 19, 9, 27, and 23 are not effective EPO mimetics and provides no evidence that SEQ ID NO:8 is capable of neuroprotective activity. The Bernaudin and Campana references are not directed to the EPO mimetics of the present invention but to EPO or truncated EPO. In stark contrast, the present application demonstrates that SEQ ID NOS: 8, 19, 9, 27, and 23 are capable of promoting neurite outgrowth in cells and claims methods of using these peptides to treat conditions mediated by neurotoxicity, neurodegeneration or neurological damage. Since there is nothing suggesting that a combination of the cited references would have produced the claimed invention and there is nothing in the cited references suggesting that the claimed methods would have a reasonable expectation of success, Applicants respectfully request that the rejection for alleged obviousness be reconsidered and withdrawn.

The foregoing represents a *bona fide* attempt to advance the present case to allowance. Applicants submit that this application is now in condition for allowance. Accordingly, an indication of allowability and an early Notice of Allowance are respectfully requested.

If the Examiner believes that a telephone conference would expedite prosecution of this application, please telephone the undersigned at 215-576-0300.

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